EXHIBIT 3

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF MICHIGAN
SOUTHERN DIVISION

In re Flint Water Cases	Civil Action No. 5:16-cv-10444-JEL-MKM (consolidated) Hon. Judith E. Levy Mag. Mona K. Majzoub
Elnora Carthan, et al. v. Governor Rick Snyder, et al.	Civil Action No. 5:16-cv-10444-JEL-MKM

REBUTTAL DECLARATION OF HOWARD HU, M.D., M.P.H., Sc.D.

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I. INTRODUCTION

I, Howard Hu, M.D., M.P.H., Sc.D., state and declare as follows:

1. In my initial declaration, I presented the opinion that adult residents in Flint who ingested Flint water during the period of May 1, 2014 through October 16, 2015 had ingested water that was more likely than not capable of causing adverse health effects. That opinion was predicated on the exposure assessment work presented by Drs. Russell, Weisel and Georgopoulos.
2. I submit this rebuttal declaration in response to the declarations of several of the Defendants' witnesses.[1, 2]

[1] In this declaration, I address the primary criticisms presented by the Defense reports that responded to my initial report. However, the Defense reports totaled several hundred pages and the materials upon which those reports were based were not contemporaneously produced. Failure to rebut all statements proffered by the Defendants in their voluminous reports is not an indication that I agree with those statements not specifically addressed.

[2] At the time my rebuttal declaration was served in this case, October 18, 2022, there were nine questions certified for trial by the Court. Shortly thereafter, on October 26, 2022, it is my understanding that the certified questions were condensed and modified to five. The original question I addressed was: "Were the corrosive water conditions allegedly caused by Defendants capable of causing harm to Flint residents, property, and businesses?" The new related question is: "Were the harmful water conditions capable of causing harm to Flint residents, properties, and businesses?" This change has no impact on my original analysis, nor any of the conclusions presented in my prior reports.

II. DECLARATION OF DR. ANTHONY R. SCIALLI

1. Exposure to Flint Water in Pregnant Women

The first is Dr. Anthony R. Scialli, M.D. In his declaration dated February 3, 2023, Dr. Scialli states an opinion that "[t]he exposure of Flint residents to allegedly contaminated water during the Flint Water Crisis (April 25, 2014 to October 16, 2015) was not capable of lead exposure sufficient to cause reproductive harm" (internal footnote omitted). He cites two sources for this contention, the first being a study conducted by Gomez et al. (2019)[3] of blood lead levels among females of reproductive age (12–50 years old) over a period of time that includes intervals before, during, and after the sourcing of Flint water from the Flint River, comparing women who lived in Flint with women who lived outside of Flint in Genesee County and who had blood lead levels taken at a single hospital.

Although Gomez et al. did not find meaningful differences suggestive of increased blood lead levels among women living in Flint in the "during" period (April 25, 2014–October 15, 2015), as the authors acknowledge themselves, the study was of females of childbearing age, as opposed to pregnant females. Neither blood lead levels nor actual outcomes data from pregnant females before or during

[3] Gómez HF, Borgialli DA, Sharman M, Weber AT, Scolpino AJ, Oleske JM, Bogden JD. Blood Lead Levels in Females of Childbearing Age in Flint, Michigan, and the Water Crisis. Obstet Gynecol. 2019 Sep;134(3):628–635. doi: 10.1097/AOG.0000000000003416. PMID: 31403597.

the Flint water exposure are available for analysis. Moreover, it is important to acknowledge that the data taken over the three periods of time do not represent repeated measures of the same women; rather, the data reflect measures of groups of women who, across the three periods of time, are different from each other. As such, it remains unknown whether women across the three periods of time had similar water consumption patterns, diets, and/or other sources of potential lead exposure (e.g., occupational exposures, exposures to lead paint) that could have influenced the results. Differences in such exposure sources could have obscured any effect attributable to the "during" period of the Flint Water Crisis. Finally, and perhaps most importantly, as Gomez et al. note in the discussion section of their report, the City of Flint's financial reports document a sharp decline in total water consumption after the Flint River water switch and before the water advisory regarding lead was issued in late September 2015, indicative of a water avoidance phenomenon. As such, many of the women who contributed data on blood lead levels in the "during" period (April 25, 2014–October 15, 2015) may not have been drinking the contaminated water at all, thereby introducing what epidemiologically would be considered as misclassification of women who were unexposed as exposed, and decreasing the ability of the Gomez et al. study to have demonstrated differences in the geometric or arithmetic mean statistics in comparisons of the blood lead levels between the three periods of time.

The second source for Dr. Scialli's contention that the exposure to Flint residents was not capable of lead exposure sufficient to cause reproductive harm is a report by Rosenman et al. (2014)[4] of results from the adult blood lead epidemiology surveillance (ABLES) program in Michigan. Dr. Scialli noted that "…there was no statistically significant increase in the percentage of adults in Flint with blood lead concentration ≥ 5 µg/dL, supporting the findings of Gómez et al." However, the report found that the percentage of adults with elevated blood lead levels (≥ 5 µg/dL) increased from 11.6% prior to 16.3% after the switch among all adults, and, furthermore, increased from 5.9% prior to 9.1% after the switch among adults who had no identified work or hobby source of lead exposure. In Table 11 of the report, this can be seen to correspond to 5 of 43 adults (11.6%) prior to the switch v. 17 or 104 adults (16.3%) after the switch; and among adults without known occupational/hobby exposure source, 2 of 34 (5.9%) prior to the switch v. 8 of 88 (9.1%) after the switch. The authors note that the increase was similar to that seen in children; however, a possible explanation for the lack of statistical significance in the ABLES data was the small number of adults tested for blood lead.

[4] Roseman KD, Kica J, Pickelman B. 2014 Annual Report. Adult blood lead epidemiology surveillance (ABLES) program. July 12, 2016. https://oem.msu.edu/images/annual_reports/occupational_illness/2014ABLESReportRev.pdf

Finally, although Dr. Scialli commented on the birth outcome findings of a study by Hanna-Attisha et al. (2021)[5] of births in Flint from November 2015–January 2016 compared to births in Detroit among newborns who previously shared the same water source from May 2012–July 2012, he failed to note the umbilical cord blood lead findings, including the observation that the proportion of cord blood lead levels greater than or equal to 1 μg/dL was 7-fold higher among Flint newborns (14%), as compared with Detroit newborns (2%; p = 0.001). Although only a few of the Flint newborns had cord blood lead levels exceeding 2 ug/dL, the authors noted that the Flint samples were taken after the water contamination was publicly known, with the implication that the cord blood lead levels (and resulting fetal exposure) may have been substantially higher earlier in the Flint Water Crisis.

The bottom line is that the potential for substantial prenatal lead exposure to have occurred during the Flint Water Crisis exists. No data are available to directly address this potential during the time period of most concern; however, it is known that lead levels in Flint drinking water had increased during the Flint Water Crisis, in some cases markedly so, and that Flint residents were unaware of the lead contamination problem for many months. Moreover, given that the public hospital

[5] Hanna-Attisha M, Gonuguntla A, Peart N, LaChance J, Taylor DK, Chawla S. Umbilical Cord Blood Lead Level Disparities between Flint and Detroit. Am J Perinatol. 2021 Aug;38(S 01):e26–e32. doi: 10.1055/s-0040-1705135. Epub 2020 Mar 6. PMID: 32143224.

in Flint where Hanna-Attisha et al. conducted their study of cord blood lead levels had 99 women who gave birth during the two months of data collection (November 2015 to January 2016) and who were confirmed to live in Flint and meet other study criteria,[6] yielding an average of over 10 births per week, it is likely that there were substantial numbers of women living in Flint who were pregnant during the period of months when Flint drinking water was contaminated but before the lead contamination was known.

2. <u>The Impact of Low-Level Prenatal Lead Exposure on Reproduction</u>

Dr. Scialli then reviews a number of studies that address the association of lead exposure with adverse birth outcomes. For each one that finds a relationship between relatively low levels of lead exposure (blood lead levels <5 ug/dL), he inserts study criticisms, caveats, or other comments. Many of his remarks are mischaracterizations, misleading, or simply wrong.

For example, in paragraph 23a, he reviews Borja-Aburto et al., 1999, and then quotes a paper I published with colleagues serving on an expert panel convened by the U.S. Centers for Disease Control that noted that there were no documented short-term or long-term risks to adult health associated with blood lead levels below 5

[6] Hanna-Attisha M, Gonuguntla A, Peart N, LaChance J, Taylor DK, Chawla S. Umbilical Cord Blood Lead Level Disparities between Flint and Detroit. Am J Perinatol. 2021 Aug;38(S 01):e26-e32. doi: 10.1055/s-0040-1705135. Epub 2020 Mar 6. PMID: 32143224.

ug/dL—implying that this contradicts the assertions I made in my October 18, 2022 report. This is misleading, as the expert panel paper was published in March 2007 (Kosnett et al. (2007)), more than 15 years ago, following which a plethora of research has emerged outlining the evidence on impacts on adult health of lead exposure associated with blood lead levels below 5 ug/dL, some of which I reviewed in my October 18, 2022 report.

As another example, in paragraph 23c, Dr. Scialli reviews Ou et al. (2020), which found in a case control study that the mean blood lead level among women who experienced spontaneous terminations of pregnancies (2.717 ug/dL) was significantly higher than the mean blood lead level in the control group (1.596 ug/dL). He then asserts, "[h]owever, it is highly likely that the units for the lead concentrations were mistakenly given as µg/L rather than µg/dL based on references in this paper to values obtained in other studies. Therefore, all the values in this paragraph should be multiplied by 10 to represent µg/dL." He is basically proposing that the "true" mean blood lead level of the spontaneous abortion women v. controls was 27.17 ug/dL v. 15.96 ug/dL. This is absurd and based on a complete absence of supportive evidence. In fact, this was a population-based study conducted at Peking Union Medical College Hospital from 2016–2018. National data on blood lead levels in China have clearly shown that average blood lead levels peaked in the 1990's at around 9 ug/dL, and then fell to below 3 ug/dL by 2016. Thus, the findings

of Ou et al. (2020) are consistent with an adverse impact on reproductive health, i.e., increased risk of spontaneous abortion, at levels of blood lead below 5 ug/dL.

As another example, in paragraph 25, Dr. Scialli proceeds to review 18 studies that focused on the potential association of prenatal lead exposure and preterm delivery. The first six were published prior to 1990 and involved women who predominantly had blood lead levels greater than 5 ug/dL, making them of limited to no value in ascertaining potential risks of lead exposure associated with blood lead levels below 5 ug/dL. Dr. Scialli did not mischaracterize the seventh study (Bellinger et al.), but in his review in paragraph 25h of the next study (West et al. (1994))[7] of women whose blood lead levels during pregnancy ranged from 2.7 to 12.6 ug/dL, he summarized the findings as "[m]aternal blood lead concentration during pregnancy was not associated with birth weight or preterm delivery." However, the authors actually found inverse correlations between blood lead levels and gestational age, Ponderal index, and infant orientation. Moreover, after excluding women with genital infections, for which a considered rationale was given, the maternal blood lead levels of mothers of low-birth-weight infants were significantly higher than those of mothers who delivered infants weighing 2500g or

[7] West WL, Knight EM, Edwards CH, Manning M, Spurlock B, James H, Johnson AA, Oyemade UJ, Cole OJ, Westney OE. Maternal low level lead and pregnancy outcomes. J Nutr. 1994 Jun;124(6 Suppl):981S–986S. doi: 10.1093/jn/124.suppl_6.981S. PMID: 8201449.

more. Among the conclusions drawn by the authors themselves was the statement that the results "…indicate that even moderate levels of lead may be associated with premature delivery in African American women, as indicated by the inverse relationship between gestational age and maternal lead levels."

As another example, in paragraph 25l, Scialli reviews a study by Vigeh et al. (2011) of blood lead levels in pregnant women and associated impacts on duration of gestation. The authors found that the mean±SD values for blood lead were significantly higher in mothers who delivered preterm babies (4.46±1.86 ug/dL) than in those who delivered full-term babies (3.43±1.22 ug/dL), and that a 1 ug/dL increase in blood lead was associated with a statistically significant increased risk of preterm birth (OR 1.41, 95% CI 1.08 to 1.84) — suggesting that lead exposure associated with blood lead levels less than 5 ug/dL pose a risk of preterm birth. However, in his report, Scialli does not mention that the study relates to blood lead levels under 5 ug/dL; he states that "there was an association of maternal blood lead concentration with preterm labor, by which the authors presumably meant preterm delivery, not defined"; and then states that "[s]ocioeconomic status did not appear to have been included in the analysis[,]" — comments (or lack thereof) clearly meant to detract from the significance of the study. This is misleading, since: (a) the study is clearly relevant to the issue of risk associated with blood lead levels under 5 ug/dL; (b) the authors clearly state in the methods and results section of the paper that the

outcome of interest was preterm delivery, defined as delivery after 20 and before 37 weeks of gestation; and (c) in their analyses, the authors controlled for education, a well-known proxy for socioeconomic status in epidemiological studies of populations.

In addition, in some of the critiques Dr. Scialli levies, he downplays studies that found significant associations between low levels of blood lead (<5 ug/dL) and adverse outcomes due to the lack of adjustment for plasma volume expansion among the research subjects due to the possibility that blood lead levels in women who have a hypertensive disorder of pregnancy would therefore have artificially elevated blood lead levels. This is the case, for example, for his reviews of studies that found evidence of adverse impacts of low levels of lead (<5 ug/dL) on pregnancy outcomes in paragraphs 27c, d, f, g, i, and m; and 29a–e, f, h, and i. As justification for this particular criticism, Dr. Scialli cites a paper on physiological adaptation of maternal plasma volume during pregnancy by de Haas et al. (2017)[8] and asserts that the findings of the paper indicate that pregnancies associated with fetal growth restriction will result in artifactually higher measurements of blood lead due to hemoconcentration. A close examination of the study by de Haas vitiates Dr.

[8] de Haas S, Ghossein-Doha C, van Kuijk SM, van Drongelen J, Spaanderman ME. Physiological adaptation of maternal plasma volume during pregnancy: a systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2017 Feb;49(2):177–187. doi: 10.1002/uog.17360. PMID: 28169502.

Scialli's assumption, however. Although the investigators found in their analysis that the pooled estimate of plasma volume expansion in complicated pregnancies at 36–41 weeks was 13.3% smaller than the reference value indicated by normal pregnancies, in the Discussion section of the paper, the authors note that "[i]t may be that these women have a lower pre-pregnancy volume but the increase is comparable to that in healthy pregnancies," an assumption that "…is supported by the observation that lower non-pregnancy volume has been described in formerly PE (pre-eclampsia) women and women with recurrent delivery of growth-restricted babies." Such a situation would clearly *not* result in either hemoconcentration or artifactually higher measurements of blood lead due to hemoconcentration. Thus, the assertion that Dr. Scialli uses to undercut the significance of the studies he subjects to this criticism is without foundation.

3. The Impact of Low-Level Prenatal Lead Exposure on Offspring Cognition

In his review of cognitive outcomes among the offspring, Dr. Scialli engages in a similar series of distortions of the research, the research results, and the interpretation of the results. For example, in his review of Jedrychowski et al. (2009),[9] a study of prenatal lead exposure at low levels and cognitive outcomes at

[9] Jedrychowski W, Perera F, Jankowski J, Mrozek-Budzyn D, Mroz E, Flak E, Edwards S, Skarupa A, Lisowska-Miszczyk I. Gender specific differences in neurodevelopmental effects of prenatal exposure to very low-lead levels: the prospective cohort study in three-year olds. Early Hum Dev. 2009 Aug;85(8):503–

three years of life, Dr. Scialli acknowledges that, in the analyses conducted by the authors, mental development index (MDI) scores were associated with prenatal lead concentration in boys at 36 months, with each increase of 1 µg/dL in maternal blood lead associated with a 1-point decrease in MDI score, but then notes "…but no shift in the lower end of the distribution". As far as I'm aware, the fact that there was no shift in the lower end of the distribution of cognitive performance scores in the face of a significant downward shift in the mean of the distribution of cognitive performance scores does not detract from the public health and policy significance of the study's conclusions, regarding which the authors state "[t]he study suggests that there might be no threshold for lead toxicity in children and provides evidence that 3-year old boys are more susceptible than girls to prenatal very low lead exposure."

As another example, Scialli reviewed Emory et al. (2003), a comparison of infants born to mothers with blood lead levels less than 5 ug/dL (range: 0.05–0.72 ug/dL, mean of 0.72 ug/dL). Scialli stated that "[e]xploratory analyses were conducted rather than the analyses being determined *a priori*[,]" with the implication that without an *a priori* hypothesis, any significant findings could be the result of a "fishing expedition" rather than a true test of a hypothesis. This is simply incorrect;

10. doi: 10.1016/j.earlhumdev.2009.04.006. Epub 2009 May 17. PMID: 19450938; PMCID: PMC3725459.

the authors clearly state that their aim was to test the hypothesis that low-level lead exposure affects higher level cognitive performance, with the Fagan Test of Infant Intelligence as the measured outcome. Their analyses, in fact, confirmed the hypothesis, with infants who scored in the lower 5th to 15th percentile of novelty preference scores having significantly higher lead values than those scoring in the upper 5th or 15th percentile of novelty preference scores. The novelty preference score is calculated from the average percentage of time each infant spent looking at the novel stimulus across 10 trials. It was the main and only outcome tested, and the result of analyses being determined *a priori*, in direct contrast to Dr. Scialli's claim. Dr. Scialli also speculated that "Given the small number of subjects (12/group) and the overlap in lead measurements, it is possible that the results were influenced by outlier measurements," thereby implying that the data analyses conducted by the authors may have been compromised or suboptimal. However, the range of blood lead levels in the low-lead subjects and high-lead subjects was 0.05–1.40 ug/dL and 0.05–2.70 ug/dL, respectively. With all values below 3.0 ug/dL, it seems highly unlikely that there were "outliers" in the dataset.

This overall pattern of misrepresenting research methods and results, misleading interpretations, and obfuscation pervades Dr. Scialli's review of the literature in his report. As such, in my opinion, they render Dr. Scialli's interpretation of the scientific literature unreliable, including the conclusions he

reaches, such as that he makes with regards to the research on low-level prenatal lead exposure and offspring cognition, i.e., "[t]he published literature is inconsistent; many studies show no association between maternal blood lead concentration and cognitive performance of children." On the contrary, the published literature that is relevant to the subject is, in my opinion, quite consistent and supportive of the adverse impact of prenatal low-level lead exposure on offspring neurodevelopment.

4. <u>Lead's Transfer Across the Placenta</u>

In Paragraph 41, Dr. Scialli takes issue with my statement that lead freely crosses the placenta, stating that the assertion is not accurate. He cites, as evidence, a single study conducted by Schell et al. (2009) [10] that found that umbilical cord blood lead levels were 65–70% of the maternal blood lead concentration, suggesting some impediment to transfer. Dr. Scialli's assertion is incorrect as well as a selective interpretation of the literature. In the reference he quotes (Schell et al. (2009)), the correct comparison, seen in Table 1, is of the mean maternal blood lead at delivery (2.8 µg/dL) v. mean infant blood lead at delivery (2.3 µg/dL). The latter represents 82% of the maternal blood lead, rather than the 65–70% value described by Scialli.

[10] Schell LM, Denham M, Stark AD, Parsons PJ, Schulte EE. Growth of infants' length, weight, head and arm circumferences in relation to low levels of blood lead measured serially. Am J Hum Biol. 2009 Mar-Apr;21(2):180-7. doi: 10.1002/ajhb.20842. PMID: 18991336; PMCID: PMC3099262.

In addition, this is but one study, whereas a scan of the peer-reviewed scientific literature shows a number of other values that are similar to 82% or higher. For example, Harville et al. (2005) [11] found that the mean cord lead level was 84% of the mean maternal blood lead at delivery (2.65 v. 1.96 µg/dL); and Osman et al. (2000) [12] found that the mean cord lead level was 98% of the mean maternal blood lead at delivery (54 nmol/L v. 55 nmol/L). Finally, in the Guidelines for the Management of Lead Exposure (2010)[13] that was published by an expert Committee convened by the U.S. Centers for Disease Control and Prevention (on which I was a member), a basic Key Point is that "[l]ead readily crosses the placenta by passive diffusion and has been measured in the fetal brain as early as the end of the first trimester, so primary prevention of exposure is particularly important to reduce risk." (Page 27).

[11] Harville EW, Hertz-Picciotto I, Schramm M, Watt-Morse M, Chantala K, Osterloh J, Parsons PJ, Rogan W. Factors influencing the difference between maternal and cord blood lead. Occup Environ Med. 2005 Apr;62(4):263–9. doi: 10.1136/oem.2003.012492. PMID: 15778260; PMCID: PMC1740989.

[12] Osman K, Akesson A, Berglund M, Bremme K, Schütz A, Ask K, Vahter M. Toxic and essential elements in placentas of Swedish women. Clin Biochem. 2000 Mar;33(2):131–8. doi: 10.1016/s0009-9120(00)00052-7. PMID: 10751591.

[13] U.S. Centers for Disease Control, 2010. Lead and Pregnancy. Available at: https://www.cdc.gov/nceh/lead/publications/leadandpregnancy2010.pdf

III. DECLARATION OF DR. BRENT FINLEY

In his declaration, Dr. Finley criticizes the position that exposure to lead in the Flint Water Crisis resulted in elevated blood lead levels with a duration of exposure that is capable of causing adverse health effects.

Most of Dr. Finley's arguments pertain to sources of lead exposure. I defer to Dr. Weisel and Dr. Georgopoulos to address these arguments, given their expertise.

However, Dr. Finley also discusses two studies of blood lead levels involving Flint residents—Gomez et al. (2019) and Rosenman et al. (2014)—to support his contention that blood lead levels were not significantly elevated during the Flint Water Crisis among any individuals. As noted by Dr. Finley, Gomez et al. (2019) performed a retrospective cross-sectional analysis in which the authors assessed the geocoded blood lead levels of Flint females of childbearing age (ages 12–50 years old) during three 18-month timeframes. These timeframes included: Period I – April 25, 2012, to October 15, 2013 (before the switchover period), Period II – April 25, 2014, to October 15, 2015 (during the switchover period), and Period III – April 25, 2016, to October 15, 2017 (after the switchover period). Gomez et al. (2019) reported that the mean Flint blood lead levels actually decreased during the switchover period (from 0.69 µg/dL to 0.65 µg/dL) and concluded that "blood lead levels in Flint females of childbearing age did not increase during the Flint River water exposure and subsequent 18-month time period." However, it is important to acknowledge

that the data taken over the three periods of time (before, during, after) do not represent repeated measures of the same women; rather, the data reflect measures of groups of women who, across the three periods of time, are not the same women. As such, it remains unknown whether these three groups of different women across the three periods of time had similar water consumption patterns, diets, and/or other sources of potential lead exposure (e.g., occupational exposures, exposures to lead paint) that could have influenced the results. In other words, there was no ability to control for potential confounders. Differences in such exposure sources could have obscured any effect attributable to the "during" period of the Flint Water Crisis.

The report by Rosenman et al. (2014)[14] discussed the results from the adult blood lead epidemiology surveillance (ABLES) program in Michigan. Dr. Finley noted that "…there was no statistically significant increase in %EBLL (≥ 5 µg/dl) at any point during the switchover period, including the January-September 30, 2015 period that is relevant to this case." However, the report found that the percentage of adults with elevated blood lead levels (≥ 5 µg/dL) increased from 11.6% prior to 16.3% after the switch among all adults, and, furthermore, increased from 5.9% prior to 9.1% after the switch among adults who had no identified work or hobby source

[14] Roseman KD, Kica J, Pickelman B. 2014 Annual Report. Adult blood lead epidemiology surveillance (ABLES) program. July 12, 2016. https://oem.msu.edu/images/annual_reports/occupational_illness/2014ABLESReportRev.pdf

of lead exposure. In Table 11 of the report, this can be seen to correspond to 5 of 43 adults (11.6%) prior to the switch v. 17 or 104 adults (16.3%) after the switch; and among adults without known occupational/hobby exposure source, 2 of 34 (5.9%) prior to the switch v. 8 of 88 (9.1%) after the switch. The authors note that the increase was similar to that seen in children; however, a possible explanation for the lack of statistical significance in the ABLES data was the small number of adults tested for blood lead.

The bottom line is that the potential for substantial adult lead exposure to have occurred during the Flint Water Crisis exists. Little to no data are available to directly address this potential during the time period of most concern, such as repeated measures of blood lead among the same adults, before, during, and after the Flint Water Crisis. However, it is known that lead levels in Flint drinking water had increased during the Flint Water Crisis, in some cases markedly so; and that Flint residents were unaware of the lead contamination problem for many months. The circumstances created the conditions for significant lead exposure to have occurred among the adults.

Later in his report, Dr. Finley goes over my testimony regarding the importance of magnitude as well as duration of exposure in determining the likely full impact of a toxic exposure (such as lead) on human health. He also noted my acknowledgment, in my deposition, that I did not determine the minimum lead

dose/duration threshold for the health effects discussed. Dr. Finley then reviews many of the studies I cited as evidence of lead exposure having adverse impacts on adult health outcomes and basically argues that, based on the reported blood lead levels, they related to study populations that likely had lead exposures that exceeded that of Flint residents. The implication of his argument is that the evidence does not support that the level of lead exposure experienced by Flint residents was capable of causing adverse adult health outcomes.

There are two problems with Finley's conclusion. The first is that the data evaluating the mean lead exposure of Flint adults (as reflected by blood lead levels) is sparse and cannot be used to rule out the possibility that significant adult lead exposures with elevated blood lead levels occurred for adult class members. The Gomez et al. (2019) study involved only 84 women who had blood lead levels taken during the Flint Water Crisis and, as noted above, their comparability to the women who contributed blood lead data before and after the Flint Water Crisis is unclear. The Rosenman et al. (2014) data on adults without occupational exposures to lead actually demonstrated an increase in the % of individuals with blood lead levels >5 ug/dL during the Flint Water Crisis, but there were not enough adults tested to demonstrate that the increase was statistically significant. Rosenman's study contained only 34 adults with pre-switch blood lead data and 88 adults with post-switch blood lead data, with no data on covariates to control for potential

confounding. In short, there simply were no systematic surveys or epidemiological studies done of adult blood lead levels that were specifically designed to determine if the Flint Water Crisis was associated with increases in adult blood lead levels. Moreover, the analyses that were performed by both Gomez et al. and Rosenman et al. include both adults who ingested unfiltered drinking water during the class period and adults who ingested bottled water or filtered tap water during the class period. As Gomez et al. indicated in their paper, there was a substantial increase in the installation of water filters and a substantial reduction in the consumption of Flint water in general. Studies that fail to control for those who continued to ingest unfiltered Flint tap water with elevated levels of lead, and those who did not, will understate the magnitude of the likely increase in adult blood lead levels for class members. It is clear that water lead levels likely increased in Flint households during the Flint Water Crisis, and lead in water is well-known to be biologically available for absorption into the body and contribute to elevations in blood lead.

The second problem is that, although (a) it is unclear to what extent blood lead elevations occurred among Flint residents; (b) the duration of exposure was likely limited in any individual to a maximum of 18 months; and (c) many if not most of the epidemiological studies on low-level lead exposure and adverse outcomes involved populations that likely had low-level lead exposure that may have exceeded the magnitude and duration of lead exposures in Flint adults, it is also clear that

thresholds for lead's impacts on adults in terms of blood lead level and duration of exposure have not been established. For some of the exposure-outcome relationships, no evidence of a threshold has been seen down to a blood lead level of 1.0 ug/dL. For example, in the recent study by Lanphear et al. (2018)[15] of blood lead levels and mortality using data from the U.S. National Health and Nutrition Examination Survey, an increase in the concentration of lead in blood from 1.0 µg/dL to 6.7 µg/dL was found to be associated with all-cause mortality (hazard ratio 1·37, 95% CI 1·17-1·60), cardiovascular disease mortality (1·70, 1·30-2·22), and ischemic heart disease mortality (2·08, 1·52-2·85), with no evidence of a threshold down to a blood lead of 1.0 ug/dL.

In his report, Dr. Finley also notes that I have advocated for the use of bone lead levels as a metric that is superior to blood lead levels for assessing cumulative lead exposure. However, although I have found that measures of bone lead (using the non-invasive K-x-ray fluorescence instrument) are more strongly associated with health outcomes in some of the studies conducted by my research group, the finding certainly does NOT negate the value and importance of studies that only used blood lead levels as a biomarker of lead exposure and found that low levels of blood lead

[15] Lanphear BP, Rauch S, Auinger P, Allen RW, Hornung RW. Low-level lead exposure and mortality in US adults: a population-based cohort study. Lancet Public Health. 2018 Apr;3(4):e177-e184. doi: 10.1016/S2468-2667(18)30025-2. Epub 2018 Mar 12. PMID: 29544878.

are associated with adverse adult outcomes. Thus, although Dr. Finley undertook a modeling exercise to demonstrate that eight months of exposure to 10 parts per billion (ppb) of water lead would result in only slight increases in bone lead, the fact that eight months of exposure to 10 ppb of water lead would result in an increase in blood lead level of 0.43 ug/dL in a 50 year old female (as estimated by Dr. Georgopoulos in Table 1 of my October 18, 2022 report), in my view, is representative of a quantifiable and meaningful elevation in risk in light of studies of low level blood lead and adverse outcomes, such as the investigation of blood lead and mortality by Lanphear et al. (2018) mentioned in the paragraph above.

IV. DECLARATION OF DR. DOUG WEED

Dr. Weed's critique of my report begins with a footnote (footnote 3, page 8) that raises the question of whether I had communicated to ATSDR potential conflicts of interest at the time I served as an expert reviewer of their 2020 Toxicological Profile of Lead. The answer is yes: I shared with ATSDR that I serve as an expert witness for worker's compensation, disability, and causation cases related to occupational medicine and environmental health.

Dr. Weed then states:

> In the first version of his claims about the possible effects of lead—at ranges he describes as "within 5 or 10 µg/dL"—Dr. Hu clearly believes that lead causes adverse effects on the "functions" of five organ systems. However, when he further describes what he believes to be the evidence supporting these claims, it turns out that, in fact, Dr. Hu does

> not believe that lead's potential effect on the immune system—what he calls "perturbations of the immune system"—represents a causal association. This is a serious contradiction by Dr. Hu.

This is an attempt by Dr. Weed to split hairs and make semantic distinctions rather than evaluate the full context of my report. At pages 7–8 of my October 18, 2022 report, I stated that "[t]he scientific literature also supports the view that relatively modest elevations in blood lead levels (i.e., within 5 or 10 ug/dL) are a cause of adverse effects on neurological, renal, hematological, immunological, and reproductive functions." As an academic (currently an Adjunct Professor) as well as a consultant who clearly is very familiar with expert testimony in legal cases, Dr. Weed should know that stating that the literature "supports" is not equivalent to saying that "a causal relationship more likely than not exists." The former is equivalent to "is consistent with"; however, neither "supports" nor "is consistent with" carry the legal weight of "more likely than not". That is precisely why, in the subsequent paragraphs, I provided more detail on each of the lead-outcome relationships of relevance and then chose to say whether, in my opinion, a particular causal relationship was more likely than not present—or not.

Dr. Weed then tries to create an issue over my reference to the review of lead and hypertension published by Acien et al. (2007) as appearing in the journal published by the U.S. National Institute for Environmental Health Sciences (NIEHS) as an attempt to suggest that NIEHS formally supports a causal relationship between

lead and hypertension. That is an assumption that is false and, basically, innuendo. My reference to NIEHS publishing the journal is simply a way of underscoring the value and impact of the journal, not an attempt to suggest that NIEHS formally supported a causal relationship between lead and hypertension.

Dr. Weed then basically criticizes my report for not going through a comprehensive review of the literature on the subject of relatively low blood lead levels and increased blood pressure and/or risk of hypertension, noting that the causal claim is "built on quicksand," and that I should have "followed accepted scientific methodology and systematically reviewed this more recent evidence." He then provides a bullet list of components of a systematic review.

It is true that I did not attempt to do such a systematic review. The reason is that it was not necessary, given that others had already conducted such reviews. Here, I am not only referring to Acien et al. (2007), but also (a) an authoritative publication that was issued in 2012 by the National Toxicology Program (NTP), which is a branch of NIEHS (which is ironic, given Dr. Weed's previous criticism of how I characterized the article by Acien et al.); and (b) an authoritative publication that was issued by the U.S. Environmental Protection Agency (EPA) in 2013. In addition, the 2020 report of the Agency for Toxic Substances and Disease Registry (ATSDR) conducted thorough literature searches from 2013 to 2019 (i.e., after the NTP and EPA reports were issued) to identify studies published since 2013 and

applied a set of rigorous criteria in consideration of which studies to include in the Profile (see ATSDR document Appendix B). And the prior NTP and EPA publications conducted even more comprehensive reviews of the literature than the subsequent ATSDR review, as noted in their description of methodology.

With regards to the NTP, in its 2012 monograph, "*The Health Effects of Low-Level Lead*", the NTP concluded the evidence is sufficient to conclude that the health effects of low-level lead exposure (<10 ug/dL) include increased blood pressure and increased risk of hypertension.[16] The NTP's conclusions were based on an extensive process. In its comprehensive review of the literature review, the quality of individual studies was considered in reaching health effects conclusions—including consideration of known confounders, appropriateness of the method of diagnosis, strength of the study design, and the sample size. General strengths and limitations of study designs were considered when developing conclusions, with prospective studies providing stronger evidence than cross-sectional or case-control studies. Consistency of effects across the body of evidence and important factors such as the number of studies, exposure levels, biological plausibility, and support from the animal literature were all assessed when developing the NTP conclusions. The NTP also considered other authoritative government evaluations of the health effects of

[16] NTP. *Health Effects of Low-Level Lead*. 2012. Office of Health Assessment and Translation, the National Toxicology Program. U.S. National Institute of Environmental Health Sciences, Research Triangle Park, NC. Table 1.1, page xix.

lead, such as the 2006 U.S. Environmental Protection Agency's (EPA) Air Quality Criteria Document for lead, which itself had gone through extensive peer review. The NTP's process also benefited from the input of a set of technical advisors, and the input on drafts of its report by a panel of reviewers with expertise in lead or metals related to reproductive and developmental toxicology, neurotoxicology, immunotoxicology, cardiovascular toxicology, renal toxicology, and exposure. Public comments were also received and considered during finalization of the document.

With regards to the EPA's authoritative review, in its 2013 report, *Integrated Science Assessment for Lead*, the EPA concluded that there was a causal relationship between lead exposure and increased blood pressure and hypertension incidence[17], with a detailed discussion of the consistency of the evidence, including evidence associated with low blood lead levels (>2 ug/dL), meta-analyses of the evidence, and evidence clearly describing mode of action. The EPA's conclusions were based on a review that was arguably even more exhaustive and detailed than that of the NTP if one considers the number of expert authors, contributors and reviewers, and the oversight of the report by a Lead Review Panel of the Clean Air Scientific Advisory Committee.

[17] EPA. *Integrated Science Assessment for Lead*. 2013. Office of Research and Development. National Center for Environmental Assessment, U.S. Environmental Protection Agency, Research Triangle Park, NC. Table 1-2, page 1-17.

The 2012 and 2013 reviews by the NTP and EPA, respectively, are clearly far more comprehensive and authoritative than what either I, or Dr. Weed, could conduct as an individual. As such, given that the basic issue here is whether low-level lead exposure can cause elevations in blood pressure and hypertension, it obviates the need for either Dr. Weed or I to attempt to conduct an exhaustive review of our own; and it renders moot Dr. Weed's criticisms of Acien et al. as well as his criticism of my discussion of the evidence related to low-level lead's impact on blood pressure and hypertension. Indeed, the acceptance of the scientific community of the impact of low-level lead exposure on hypertension is precisely why, in my October 18, 2022 report, I did not dwell on the evidence relating low-level lead exposure to blood pressure/hypertension, but chose instead to discuss evidence of risk factors that may amplify the impact of low-level lead exposure on blood pressure/hypertension, such as stress, depression, and low socioeconomic status.

Dr. Weed also criticizes my opinions related to the impact of low-level lead exposure on kidney function. Here, I agree with Dr. Weed that the opinions I expressed in my October 18, 2022 report regarding the level of lead exposure that is sufficient to cause kidney dysfunction were not sufficiently clear as to whether they related to blood lead levels <5 ug/dL or greater (or equal) to 5 ug/dL. For the record, I would like to state that, in my opinion, the evidence indicates that blood lead levels <5 ug/dL or greater are, more likely than not, a risk factor for causing kidney

dysfunction. This is consistent with the conclusions expressed in the NTP monograph ("*The Health Effects of Low-Level Lead*"), which found that the evidence was sufficient to conclude that blood lead levels <5 ug/dL result in decreased glomerular filtration rate. The 2013 report by the EPA was less assured about this relationship, concluding that the evidence was suggestive of a causal relationship between lead exposure (at low levels) and reduced kidney function among adults. Although there is a disparity between these two federal agencies with respect to this point, additional research published after 2013—including those reviewed by the 2020 ATSDR report, such as Pollack et al. (2015)[18] and Harari et al., (2018)[19]—support the NTP's conclusion that blood lead levels are capable of causing kidney dysfunction in the form of decreased glomerular filtration rates at blood lead levels <5 ug/dL. I agree with the NTP's conclusion.

Finally, while on the subject of the 2012 NTP and 2013 EPA authoritative reviews, I note that the EPA report concluded that there was a likely causal

[18] Pollack AZ, Mumford SL, Mendola P, Perkins NJ, Rotman Y, Wactawski-Wende J, Schisterman EF. Kidney biomarkers associated with blood lead, mercury, and cadmium in premenopausal women: a prospective cohort study. J Toxicol Environ Health A. 2015;78(2):119-31. doi: 10.1080/15287394.2014.944680. PMID: 25424620; PMCID: PMC4246415.

[19] Harari F, Sallsten G, Christensson A, Petkovic M, Hedblad B, Forsgard N, Melander O, Nilsson PM, Borné Y, Engström G, Barregard L. Blood Lead Levels and Decreased Kidney Function in a Population-Based Cohort. Am J Kidney Dis. 2018 Sep;72(3):381-389. doi: 10.1053/j.ajkd.2018.02.358. Epub 2018 Apr 23. PMID: 29699886.

relationship between adult lead exposure and both cognitive function decrements and psychopathological effects (symptoms of depression and anxiety)—relationships that I discussed in my October 18, 2022 report. Here, again, there is a disparity between the two federal agencies with respect to this point, with the 2012 NTP report concluding that the evidence for lead causing decreased cognitive function and psychological effects was limited. However, in this case, I agree with the EPA's conclusion that the evidence is sufficiently in favor of low-level lead exposure as a risk factor for declines in cognitive function and psychopathological effects based on the accrual of additional relevant studies published after 2013. They include, for example: (a) a 2014 study of lead-exposed women with relatively low blood lead levels (geometric mean of 4.1 ug/dL) v. controls (geometric mean of 2.0 ug/dL) that showed, in the lead-exposed women, poorer working memory performance during high memory loading task, and on functional MRI testing, reduced activation in the dorsolateral prefrontal cortex, ventrolateral prefrontal cortex, pre supplementary motor areas, and inferior parietal cortex;[20] (b) a 2017 study using NHANES data that demonstrated an association between low blood lead

[20] Seo J, Lee BK, Jin SU, Park JW, Kim YT, Ryeom HK, Lee J, Suh KJ, Kim SH, Park SJ, Jeong KS, Ham JO, Kim Y, Chang Y. Lead-induced impairments in the neural processes related to working memory function. PLoS One. 2014 Aug 20;9(8):e105308. doi: 10.1371/journal.pone.0105308. PMID: 25141213; PMCID: PMC4139362.

levels (<5 ug/dL) and lower cognitive functioning;[21] and (c) a 2017 study of individuals with low blood lead levels (<5 ug/dL) that found an interaction between blood lead and blood cadmium levels that accounted for lower scores on working memory.[22]

V. DECLARATION OF DR. MICHAEL GREENBERG

In his declaration, Dr. Greenberg spends the initial part of the document discussing and providing his interpretation of the statements made in the 2020 ATSDR *Toxicological Profile on Lead.*

He then provides a critique of opinions I offered in my October 18, 2022 report. I will address each of the apparent critiques:

> "3: *Dr. Hu has not offered a diagnosis of any actual injury or condition regarding the so called "Flint water crisis*".

Response: My charge was to address the following question: "Were the corrosive water conditions allegedly caused by Defendants capable of causing harm

[21] Przybyla J, Houseman EA, Smit E, Kile ML. A path analysis of multiple neurotoxic chemicals and cognitive functioning in older US adults (NHANES 1999-2002). Environ Health. 2017 Mar 7;16(1):19. doi: 10.1186/s12940-017-0227-3. PMID: 28270159; PMCID: PMC5341442.

[22] Souza-Talarico JN, Marcourakis T, Barbosa F Jr, Moraes Barros SB, Rivelli DP, Pompéia S, Caramelli P, Plusquellec P, Lupien SJ, Catucci RF, Alves AR, Suchecki D. Association between heavy metal exposure and poor working memory and possible mediation effect of antioxidant defenses during aging. Sci Total Environ. 2017 Jan 1;575:750-757. doi: 10.1016/j.scitotenv.2016.09.121. Epub 2016 Sep 23. PMID: 27670596.

to Flint residents?" I addressed the question by acknowledging the levels of lead exposure that could have been experienced by some of the Flint residents, based on what was known about the corrosive water conditions and likely impacts on lead contamination and, in turn, blood lead levels (as estimated by Drs. Weisel and Georgopoulos); and then, outlining, in my opinion, the potential adverse impacts on blood pressure, risk of hypertension, renal function, cognition, and other outcomes. These are well-known "harms." I was not asked to diagnose specific diseases in any resident of Flint.

> *"4. Plaintiff's expert Dr. Howard Hu did not research into how any Flint, Michigan residents' blood pressure compares to that of the general population."*

Response: My report addresses exposure to elevated levels of lead in water and whether such exposure is capable of causing adverse outcomes, including high blood pressure and hypertension. Dr. Greenberg fails to identify population blood pressure data that should have been considered in addressing this question or how it should have been used to evaluate the general causation question.

> *"5. Plaintiffs' expert Dr. Howard Hu admits to the fact that even if a certain level of lead can cause hypertension that does not mean that it will cause hypertension."*

Response: I fail to see the relevance of this criticism. The same is true for any known risk factor-adverse outcome relationship, such as smoking and lung cancer.

No individual who has a known risk factor has a 100% chance of developing the adverse outcome that the risk factor is known to cause. However, being exposed to a risk factor will increase the probability of the adverse outcome that the risk factor is known to cause; conversely, avoiding or reducing a risk factor, such as lead exposure, will decrease the chances of developing the associated adverse outcome (in this case, hypertension).

> *"6. Plaintiff's expert Dr. Howard Hu admits that with respect to all the different conditions and injuries he discusses in his report that the relationship between the conditions and injury and lead exposure is probabilistic and not deterministic."*

Response: This issue is basically the same as the issue Dr. Greenberg posed just above. My response is basically the same. Risk factors, by definition, are not typically deterministic— i.e., the existence of a risk factor does not mean that an individual will proceed to have an adverse condition with 100% certainty. However, being exposed to a risk factor will increase the probability of the adverse outcome that the risk factor is known to cause; conversely, avoiding or reducing a risk factor, such as lead exposure, will decrease the chances of developing the associated adverse outcome.

> *"7. Plaintiffs' expert Dr. Howard Hu does not opine if any of the Flint residents actually have been diagnosed with one or more conditions he has identified as being associated with lead exposure or that lead was the cause for those conditions."*

Response: True enough, because formulating such opinions was not my charge or relevant at this stage of the proceedings. My testimony addresses the general causation relationship between the elevated lead levels in Flint water and the adverse health outcomes that such elevated lead levels are capable of causing.

> *"8. Plaintiffs' expert Dr. Howard Hu testified (Hu deposition, page 124) that the ATSDR (in a document in which he served as one of three primary reviewers) did not use the term "causality of "cause" regarding hypertension and increases in blood lead levels below 5 micrograms per deciliter".*

Response: First, it is important to note that scientific statements have ways of expressing that a risk factor is a cause of an adverse outcome that do not require using the terms "causality" or "cause." For example, in the 2012 NTP Monograph "*The Health Effects of Low-Level Lead*", the NTP concluded the evidence is "sufficient" to conclude that "the health effects of low-level lead exposure" (<10 ug/dL) include increased blood pressure and increased risk of hypertension.[23] There is no debate as to the meaning of NTP's conclusion on this matter, despite the fact that the terms "causality" and "cause" were not used. Second, in the publication by the EPA of its 2013 report, "*Integrated Science Assessment for Lead*", the EPA concluded explicitly that there was a causal relationship between lead exposure and

[23] NTP. *Health Effects of Low-Level Lead*. 2012. Office of Health Assessment and Translation, the National Toxicology Program. U.S. National Institute of Environmental Health Sciences, Research Triangle Park, NC. Table 1.1, page xix.

increased blood pressure and hypertension incidence,[24] with a detailed discussion of the consistency of the evidence, including evidence associated with low blood lead levels (>2 ug/dL), meta-analyses of the evidence, and evidence clearly describing mode of action. Their discussion of that evidence as well as the evidence discussed in the 2020 ATSDR document is persuasive, in my opinion, that blood lead levels below 5 ug/dL can cause increases in blood pressure as well as hypertension.

> *"9. Plaintiffs' expert Dr. Howard Hu testified (Hu deposition, page 125) that there are no studies showing causation regarding hypertension and increases in blood lead levels below 5 micrograms per deciliter.*

Response: Dr. Greenberg interprets my comments out of context. In my deposition, I was asked: "What studies, if any, have found causation for higher blood lead levels at blood lead levels less than 5 micrograms per deciliter?" I then responded: "Well, like I said, no individual study shows causation, but they can show associations and I've listed a bunch of them in my report". To place that in context, what I said just prior to the defense attorney's question was: "So epidemiology studies can only really demonstrate associations and then it has to be viewed in the context of all of the other epi studies and the basic science studies, the mechanistic studies, and if you will, the principles that are -- that we discussed earlier, such as

[24] EPA. *Integrated Science Assessment for Lead*. 2013. Office of Research and Development. National Center for Environmental Assessment, U.S. Environmental Protection Agency, Research Triangle Park, NC. Table 1-2, page 1-17.

those set forth by the Bradford Hill criteria, in order to formally arrive at an opinion regarding causality." Thus, Dr. Greenberg's question itself is a nonsensical question. There are no studies showing causation regarding hypertension and increases in blood lead levels below 5 micrograms per deciliter because studies by themselves do not show causation. Causation is determined based on a review of multiple studies, including epidemiological studies, basic science studies, mechanistic studies, etc., and assembling and integrating the evidence to arrive at conclusions.

> *"11. In his Declaration document, Plaintiffs' expert Dr. Howard Hu has failed to consider literature that does not agree with his stated opinions. Specifically, he has not addressed articles published by Gomez et al. (2019). This investigator reports data supporting the fact that blood lead levels in Flint females of childbearing age did not increase during the Flint River water exposure and subsequent 18-month time period."*

Response: Although the paper by Gomez et al. (2019)[25] that focused on females of childbearing age did not find meaningful differences suggestive of increased blood lead levels among women living in Flint in the "during" period (April 25, 2014–October 15, 2015), it is important to acknowledge that the data taken over the three periods of time do not represent repeated measures of the same

[25] Gómez HF, Borgialli DA, Sharman M, Weber AT, Scolpino AJ, Oleske JM, Bogden JD. Blood Lead Levels in Females of Childbearing Age in Flint, Michigan, and the Water Crisis. Obstet Gynecol. 2019 Sep;134(3):628-635. doi: 10.1097/AOG.0000000000003416. PMID: 31403597.

women; rather, the data reflect measures of groups of women who, across the three periods of time, are different from each other. As such, it remains unknown whether women across the three periods of time had similar water consumption patterns, diets, and/or other sources of potential lead exposure (e.g., occupational exposures, exposures to lead paint) that could have influenced the results. Differences in such exposure sources could have obscured any effect attributable to the "during" period of the Flint Water Crisis. In addition, and perhaps most importantly, as Gomez et al. note in the discussion section of their report, the City of Flint's financial reports document a sharp decline in total water consumption after the Flint River water switch and before the water advisory regarding lead was issued in late September 2015, indicative of a water avoidance phenomenon. As such, many of the women who contributed data on blood lead levels in the "during" period (April 25, 2014–October 15, 2015) may not have been drinking the contaminated water at all, thereby introducing what epidemiologically would be considered as misclassification of women who were unexposed as exposed, and decreasing the ability of the Gomez et al. study to have demonstrated differences in the geometric or arithmetic mean statistics in comparisons of the blood lead levels between the three periods of time.

The bottom line is that the potential for substantial prenatal lead exposure to have occurred during the Flint Water Crisis exists. No data are available to optimally address this potential during the time period of most concern; however, it is known

that lead levels in Flint drinking water had increased during the Flint Water Crisis, in some cases markedly so; and that Flint residents were unaware of the lead contamination problem for many months.

> *"12. In addition to what is described in item 11 above, Plaintiffs' expert Dr. Howard Hu has failed to consider another article published by Gomez et al. (2019) which concluded "Analyses of geometric mean and percentages greater than or equal to 5.0 micrograms per deciliter of blood lead levels do not support the occurrence of a global increase in blood lead levels in young children of Flint during the entire 18-month period of Flint River water exposure."*

Response: First of all, with respect to the approach taken by Gomez et al. in their paper on blood lead levels in children (2019),[26] the comparison of Period I (April 24, 2006 to October 15, 2007; the "earliest 18 month timeframe for which there were BLL records available to review") with Period III (April 25, 2014 to October 15, 2015; "the switchover period) for the purposes of extrapolating whether the switchover was associated with an increase in blood lead levels is spurious. Period I was eight years prior to Period III, a time interval during which blood lead levels were falling both in Flint (as demonstrated by Gomez et al. in a previous paper

[26] Gómez HF, Borgialli DA, Sharman M, Shah KK, Scolpino AJ, Oleske JM, Bogden JD. Analysis of blood lead levels of young children in Flint, Michigan before and during the 18-month switch to Flint River water. Clin Toxicol (Phila). 2019 Sep;57(9):790-797. doi: 10.1080/15563650.2018.1552003. Epub 2019 Mar 14. PMID: 30871386.

published in 2018, Figures 1 and 2)[27] and nationally (as demonstrated by Tsoi et al. (2016) in their analysis of children's blood lead levels using data from the U.S. National Health and Nutrition Examination Survey (1999–2014), the percentage of children with blood lead levels greater than 5 µg/dL fell from around 3% (2007–2008) to <1% (2013–2014), Figure 2).[28] The relevant period of comparison would have been the time period immediately prior to the switch, i.e., October 2012 to April 2014; however, these data were noted by Gomez et al. in their article to be "not available". Second, Gomez et al. (2019) actually noted that, in comparing Period II to Period III, the percentage of children with BLLs greater than 5 µg/dL had actually increased, from 3.3% to 3.9%. The major point that Gomez made was that, while the percentage of children with BLLs had increased with the switch, the geometric mean BLL fell (from 1.47 to 1.32 µg/dL). However, even here, there are important limitations to the analysis. A key one, acknowledged by Gomez et al. in the paper's discussion, is that their data, which stem from data gathered by Hurley Medical Center, account for only half of the BLLs in Flint children during the time period of

[27] Gómez HF, Borgialli DA, Sharman M, Shah KK, Scolpino AJ, Oleske JM, Bogden JD. Blood Lead Levels of Children in Flint, Michigan: 2006-2016. J Pediatr. 2018 Jun;197:158-164. doi: 10.1016/j.jpeds.2017.12.063. Epub 2018 Mar 26. PMID: 29599069.

[28] Tsoi MF, Cheung CL, Cheung TT, Cheung BM. Continual Decrease in Blood Lead Level in Americans: United States National Health Nutrition and Examination Survey 1999-2014. Am J Med. 2016 Nov;129(11):1213-1218. doi: 10.1016/j.amjmed.2016.05.042. Epub 2016 Jun 21. PMID: 27341956.

their analysis. Another key limitation is that Period III did not distinguish between the early post-switch period prior to the boil water advisory, when residents were mostly unaware of the lead contamination problem, and the later post-switch period after the boil advisory was issued. It also did not attempt to examine the continuing trend in BLLs after the drinking water source reverted to the Detroit Water Authority.

By contrast, in the analysis of blood lead levels among children in Flint, 2013–2016, conducted by Kennedy et al. (2016)[29] of the U.S. Centers for Disease Control and Prevention, the investigators were able to access all of the available BLL data for Flint children. In addition, their data set included BLL data just prior to the switch (as opposed to 8 years prior to switch, as was the case with the Gomez et al. (2019) paper), as well as data after the Flint water source was switched back to the Detroit Water Authority (DWA). In their analysis of pre-switch (April 25, 2013 to April 24, 2014) v. post-switch (April 25, 2014–January 2, 2015) BLLs, Kennedy et al. found that the percentage of BLLs greater than 5 µg/dL rose from 3.1 to 5.0%, which was associated with a statistically significant increase in the probability of having a BLL great than 5 µg/dL as reflected by an odds ratio, after controlling for

[29] Kennedy C, Yard E, Dignam T, Buchanan S, Condon S, Brown MJ, Raymond J, Rogers HS, Sarisky J, de Castro R, Arias I, Breysse P. Blood Lead Levels Among Children Aged <6 Years - Flint, Michigan, 2013-2016. MMWR Morb Mortal Wkly Rep. 2016 Jul 1;65(25):650-4. doi: 10.15585/mmwr.mm6525e1. PMID: 27359350.

covariates, of 1.46 (95% confidence interval: 1.06–2.01). They also found that after the switch back to DWA water, the percentage of elevated BLLs returned to levels comparable to those found before the water source switch.

Finally, with respect to examining measures of central tendency (mean, median, geometric mean), I note that the authors of Zahran et al. (2017),[30] like the investigators from the CDC, were also able to access the full dataset of BLLs in Flint children as well as the most relevant associated time periods. In their analysis, they found that mean BLLS increased by 0.445 µg/dL (95% confidence interval: 0.249 to 0.642) comparing the period prior to the switch (January 1, 2013 to April 25, 2014) to after the switch (April 26, 2014 to September 14, 2014). Even more telling was their finding that BLLs in Flint children living in high-risk areas (residing within one mile of spatially targeted boil water advisory areas) increased by 0.64 µg/dL (95% confidence interval: 0.395 to 0.883). After the switch back to DWA water, the children's BLLs returned to pre-switch levels, further implicating the Flint Water Crisis-associated water lead exposure as a significant contributing source of lead to children's BLLs throughout the Flint Water Crisis. It is important to note that these analyses of time trends in blood lead levels in Flint did not distinguish children who actually drank unfiltered Flint water during the period of contamination v. children

[30] Zahran S, McElmurry SP, Sadler RC. Four phases of the Flint Water Crisis: Evidence from blood lead levels in children. Environ Res. 2017 Aug;157:160-172. doi: 10.1016/j.envres.2017.05.028. PMID: 28570960; PMCID: PMC5538017.

who did not. Thus, in my opinion, it is more likely than not that the associated estimates of increases in BLLs actually underestimate the true increase in BLLs that occurred in children who drank unfiltered water in Flint.

In short, the Gomez et al. (2019) paper on children was not discussed in my October 18, 2022 declaration because its methodology and applicability to understanding the true impact of the water switch on BLLs among Flint children is limited. In contrast, the data from Kennedy et al. (2016) and Zahran et al. (2017) are methodologically more rigorous in addressing the same question and support the conclusion that increases in BLLs occurred in association with the Flint Water Crisis. Given that the children lived in the same household as their parent and/or other adults, it is likely that the blood lead levels in some of the adults increased as well.

> *"14. Plaintiffs' expert Dr. Howard Hu has failed to consider the short duration and transient nature of the purported exposure in the matter at hand."*

Response: In terms of assessing risks associated with exposure to lead, the metric used is the level of lead in blood, which, in turn, has been the metric used to estimate lead exposure in the vast majority of epidemiological studies of lead exposure and potential adverse health effects. With regards to the toxicodynamics of blood lead levels, it is clear that blood lead levels increase rapidly (within days) after exposures to lead (or increases in exposures to lead above any "baseline"

exposure). What is also known is that blood lead levels have a half-life of around 35 days (reflecting, largely, the turnover of red cells, onto which >98% of lead in blood tends to bind), unless the exposures have been ongoing for many months, in which case the decline in blood lead levels tends to be slower, since the longer exposure time would result in accumulation of lead in other soft tissues as well as the skeleton, which would then serve as a source of lead going into blood over time. As such, epidemiological studies using blood lead levels to assess exposure in relation to potential adverse health effects have rarely tried to distinguish whether the subjects being studied had been exposed for weeks, months, or years. To do so would require a comprehensive program of environmental sampling and/or weekly or monthly measurements of lead in blood over the period of potential exposure—an approach that would arguably be impossible based on ethical concerns given the mandate to intervene should untoward lead exposures be identified. In any case, in my opinion, given that the window of exposure time of relevance to the Flint Water Crisis in this case is at least 6 months or more, there is ample opportunity for individuals to have been exposed long enough for blood lead levels to have risen and remained elevated long enough to be associated with adverse health effects.

> *"(p. 22): Dr. Hu incorrectly overstates the scientific literature when he notes "supports the view that relatively modest elevations in blood lead are a cause of adverse effect on the neurological, renal, hematological, immunological and reproductive functions."*

In this paragraph, and in the subsequent three paragraphs, Dr. Greenberg generally criticizes my not having quoted specific scientific literature, or my having quoted the 2020 ATSDR document, in support of my opinions. Rather than go into a long discussion of the scientific literature, I point out that the 2020 ATSDR document itself builds upon both the 2012 National Toxicology Program monograph, "*The Health Effects of Low-Level Lead"*, and the 2013 Environmental Protection Agency Report, "*Integrated Science Assessment for Lead"*.

In its 2012 monograph, "*The Health Effects of Low-Level Lead*", the NTP determined the evidence is sufficient to conclude that the health effects of low-level lead exposure (<10 ug/dL) include increased blood pressure and increased risk of hypertension.[31] The NTP's conclusions were based on an extensive process. In its comprehensive review of the literature review, the quality of individual studies was considered in reaching health effects conclusions, including consideration of known confounders, appropriateness of the method of diagnosis, strength of the study design, and the sample size. General strengths and limitations of study designs were considered when developing conclusions, with prospective studies providing stronger evidence than cross-sectional or case-control studies. Consistency of effects across the body of evidence and important factors such as the number of studies,

[31] NTP. *Health Effects of Low-Level Lead*. 2012. Office of Health Assessment and Translation, the National Toxicology Program. U.S. National Institute of Environmental Health Sciences, Research Triangle Park, NC. Table 1.1, page xix.

exposure levels, biological plausibility, and support from the animal literature were all assessed when developing the NTP conclusions. The NTP also considered other authoritative government evaluations of the health effects of lead, such as the 2006 U.S. Environmental Protection Agency's (EPA) Air Quality Criteria Document for lead, which itself had gone through extensive peer review. The NTP's process also benefited from the input of a set of technical advisors and the input on drafts of its report by a panel of reviewers with expertise in lead or metals related to reproductive and developmental toxicology, neurotoxicology, immunotoxicology, cardiovascular toxicology, renal toxicology, and exposure. Public comments were also received and considered during finalization of the document.

With regards to the EPA's authoritative review, in its 2013 report, "*Integrated Science Assessment for Lead*", the EPA concluded that there was a causal relationship between lead exposure and increased blood pressure and hypertension incidence,[32] with a detailed discussion of the consistency of the evidence, including evidence associated with low blood lead levels (>2 ug/dL), meta-analyses of the evidence, and evidence clearly describing mode of action. The EPA's conclusions were based on a review that was arguably even more exhaustive and detailed than that of the NTP if one considers the number of expert authors, contributors and

[32] EPA. *Integrated Science Assessment for Lead*. 2013. Office of Research and Development. National Center for Environmental Assessment, U.S. Environmental Protection Agency, Research Triangle Park, NC. Table 1-2, pages 1–17.

reviewers and the oversight of the report by a Lead Review Panel of the Clean Air Scientific Advisory Committee.

The 2012 and 2013 reviews by the NTP and EPA are clearly comprehensive and authoritative. As such, given that the basic issue here is whether low-level lead exposure can cause elevations in blood pressure and hypertension, it obviates the need for me to conduct an exhaustive review of our own; and it renders moot Dr. Greenberg's criticisms of my discussion of the science. Indeed, the acceptance of the scientific community of the impact of low-level lead exposure on hypertension is precisely why, in my October 18, 2022 report, I did not dwell on the evidence relating low-level lead exposure to blood pressure/hypertension, but chose instead to discuss evidence of risk factors that may amplify the impact of low-level lead exposure on blood pressure/hypertension, such as stress, depression, low socioeconomic status. In addition, although the 2020 report of the Agency for Toxic Substances and Disease Registry (ATSDR) on the Toxicology for Lead (2020) [33] did not conduct as comprehensive a review of lead research as did the NTP or EPA in their 2012 and 2013 reports, respectively, as noted in their description of methodology, the ATSDR conducted thorough literature searches from 2013 to 2019 (i.e., after the NTP and EPA reports were issued) to identify studies published since

[33] ATSDR. *Toxicological Profile for Lead.* 2020. Agency for Toxic Substances and Disease Registry. Centers for Disease Control and Prevention. U.S. Department of Health and Human Services. Atlanta, GA.

2013 and applied a set of rigorous criteria in consideration of which studies to include in the Profile (see ATSDR document, Appendix B). That is why I chose to refer to the 2020 ATSDR document.

As for outcomes other than elevated blood pressure and risk of hypertension, the 2013 EPA report also concluded that, among adults, there is a likely causal relationship between lead exposure and cognitive function decrements, psychopathological effects, coronary heart disease, atopic and inflammatory responses, decreased host resistance, decreased red cell survival and function, altered heme synthesis, delayed puberty onset, impaired male reproductive function, and cancer (Table ES-1). In its summary (Table 1.1), the NTP report determined that the evidence was sufficient to conclude that, among adults, blood lead levels <5 ug/dL caused decreased renal function (in the form of glomerular filtration) and reduced fetal growth, and, among adults with blood lead levels <10 ug/dL, increased incidence of essential tremor (and, as noted earlier, increased blood pressure and risk of hypertension).

In summary, the literature on lead toxicity is vast. The 2020 ATSDR Toxicological Profile of Lead itself, which I used as one of my sources to illustrate what is known about lead toxicity, builds upon previous authoritative reviews by the NTP and EPA that are comprehensive in identifying the most important studies, weighing the evidence, and drawing conclusions regarding causality. As such, Dr.

Greenberg's criticism that I overstated the literature regarding the neurological, renal, hematological, immunological and reproductive impacts of lead is moot.

VI. DECLARATION OF DR. WILLIAM BANNER

In his declaration, Dr. Banner states the following:

> Dr. Hu has relied upon the total blood lead concentration rather than an increment from the water change as though they would remain elevated and thus be similar to the literature of lifetime exposures as described in the literature. What he fails to offer is that even if there were a transient increase in blood lead level, none of the existing literature on long-term health effects or cognitive impairment contemplate a short-term exposure involving low blood lead levels, with a rapid return to pre-change levels as would be predicted by the multi compartment model and the measurement of blood lead levels after changing the water back.

Response: With regards to the toxicodynamics of blood lead levels, it is clear that blood lead levels increase rapidly (within days) after exposures to lead (or increases in exposures to lead above any "baseline" exposure). Once exposure ceases, blood lead levels have a half-life of around 35 days (reflecting, largely, the turnover of red cells, onto which >98% of lead in blood tends to bind), unless the exposures have been on-going for many months, in which case the decline in blood lead levels tends to be slower, since the longer exposure time would result in accumulation of lead in other soft tissues as well as the skeleton, which would then serve as a source of lead going into blood over time. Dr. Banner appears to have made the assumption that the scientific literature on lead epidemiological studies

involves populations that have had lifetime exposures to lead. In fact, such epidemiological studies have rarely tried to distinguish whether the subjects being studied had been exposed for weeks, months, or years. Most have involved blood lead analyses taken at only a single moment in time for each individual, studied in relation to contemporaneous measures of health outcomes, or in relation to prospectively experienced health outcomes. To conclude that each individual has had a "lifetime" of exposures— or any extended period of exposure— at the same level would require a comprehensive program of environmental sampling and/or weekly or monthly measurements of lead in blood over the period of potential exposure— an approach that has rarely been taken in the research relevant to the outcomes discussed in my report. It would also arguably be complicated based on ethical concerns given the mandate to intervene should untoward lead exposures be identified. In any case, in my opinion, given that the window of exposure time of relevance to the Flint Water Crisis in this case is at least 6 months or more, there is ample opportunity for individuals to have been exposed long enough for blood lead levels to have risen and remained elevated long enough to be associated with adverse health effects.

VII. CONCLUSION

This ends my rebuttal declaration in response to the declarations of several of the Defendants' witnesses. Each of my opinions are given with a reasonable degree of scientific certainty based upon a preponderance of the evidence.

I declare under penalty of perjury that the foregoing is true and correct to the best of my knowledge and recollection.

Executed this 28th day of February, 2023, in Los Angeles, CA

By: _____

Howard Hu, M.D., M.P.H., Sc.D.